

REMARKS

Claims 1, 2, 11, 12, 15 – 17, 20 – 28, 31 – 34 and 37 – 39 are pending. Claims 1, 11, 12, 15, 17, 23, 26 – 28 and 34 have been amended and claims 2, 16, 22, 24 and 32 have been cancelled. Entry of the foregoing amendments and claim cancellations is respectfully requested.

I. Rejection of claims 1, 2, 11, 12, 15 – 17 and 20 – 25 under 35 U.S.C. § 112, first paragraph

On page 3, of the Office Action the Examiner has rejected claims 1, 2, 11, 12, 15 – 17 and 20 – 25 under 35 U.S.C. § 112, first paragraph. Applicants address the Examiner's rejections in the order a) through e), as they appear on pages 4 - 7 of the Office Action.

a) In light of the foregoing amendments to claim 1, Applicants assert that the enablement rejection has been rendered moot. Specifically, claim 1 has been amended such that it recites specific diseases and conditions originally set forth in claim 22. Reconsideration and withdrawal of this rejection is respectfully requested.

With respect to the rejection of claims 22 and 23, Applicants respectfully traverse. Claim 22, specifically recites cancer or a fibrotic disorder as the abnormal condition to be treated by the method of the claim. Claim 23, depends from claim 22 and further lists a series of specific diseases. Thus, these claims are not directed to "any and all diseases and/or disorders associated with serine/threonine protein kinase" as the Examiner indicates. Instead, the claims are directed to a very specific group of diseases or disorders, for which there is sufficient enablement in the specification as filed. As such, Applicants respectfully submit that the subject matter of claims 22 and 23 is enabled to its full scope and request the Examiner to reconsider and withdraw the 112 rejection of the subject matter of these claims.

b) Prevention

In light of the amendments to claim 17, the rejection under 35 U.S.C. § 112, first paragraph of claims 17 and 20 – 25 has been rendered moot. Specifically, claim 17, from which claims 20 – 25 depend, no longer recites "prevention." Reconsideration and withdrawal of this rejection is respectfully requested.

c) Abnormal Condition

In light of the amendments to claim 17, the rejection under 35 U.S.C. § 112, first paragraph of claims 17 and 20 – 25 has been rendered moot. Specifically, claim 17, from which claims 20 – 25 depend, now specifies the abnormal conditions contemplated in claim 17, namely “a disease associated with an aberration in a signal transduction pathway characterized by an interaction between a serine/threonine protein kinase and a natural binding partner.” Reconsideration and withdrawal of this rejection is respectfully requested.

As explained in Section (a), above, claims 22 and 23 recite specific diseases or disorders that are known in the art at this time and the time the application was filed. Therefore, these diseases do not fall within the characterization of “diseases and/or disorders not even known at the time.” Applicants submit that the subject matter of claims 22 and 23 is fully enabled and request that the Examiner to reconsider and withdraw the 112 rejection of the subject matter of these claims.

d) Definition of Z' in claim 27

In light of the amendments to claim 27, Applicants assert that this rejection has been rendered moot. Specifically, Applicants have amended claim 27 to correct an obvious clerical error in which the term “carbon” was inadvertently included in the definition of Z'. Reconsideration and withdrawal of this rejection is respectfully requested.

e) Compounds where A₁ or Z' is sulfur or oxygen

In light of the amendments to claims 1, 11, 17, 26, 27 and 34, Applicants assert that this rejection has been rendered moot. Specifically, Applicants have amended the aforementioned claims such that (i) A₁ can only be carbon or nitrogen; (ii) Z' in claims 1, 17 and 26 can only be carbon or nitrogen; and (iii) Z' in claims 11 and 27 can only be nitrogen. Reconsideration and withdrawal of this rejection is respectfully requested.

II. Rejections of Claims 1, 2, 11, 12, 15 – 17, 20 – 28, 32 – 34 and 37 - 39 under 35 U.S.C. § 112, Second Paragraph

On page 7, of the Office Action the Examiner has rejected claims 1, 2, 11, 12, 15 – 17, 20 – 28, 32 – 34 and 37 - 39 under 35 U.S.C. § 112, second paragraph. Applicants address the Examiner's rejections in the order a) through t), as they appear on pages 7 - 10 of the Office Action.

a) Proviso where A₁ is not substituted

In light of the amendments to claims 1, 11, 17, 26, 27 and 34, Applicants assert that this rejection is moot. Specifically, the aforementioned claims recite that A₁ is nitrogen or carbon and do not recite the presence/absence of any substituents on A₁.

b) Meaning of “quinazoline ring” not known

In light of the amendments to claims 1, 26 and 27, Applicants assert that this rejection is moot. Specifically, these claims recite “quinazoline-based compound,” instead of “quinazoline ring.” Support for the term “quinazoline-based compound” may be found on page 9, lines 18 – 22.

c) Meaning of “comprises two carbon atoms of quinazoline ring” not known

In light of the amendments to claims 1, 26 and 27, Applicants assert that this rejection is moot. Specifically, these claims recite “quinazoline-based compound,” instead of “quinazoline ring.” Support for the term “quinazoline-based compound” may be found on page 9, lines 18 – 22.

d) Definition of “n” not in the alternative

In light of the amendments to claims 11 and 27, Applicants assert that this rejection is moot. Specifically, these claims have been amended to correct an obvious clerical error, such that the definition of n is in the alternative.

e) Not sufficient antecedent basis in claim 1 for (v) OX₇ in claim 11

In light of the amendments to claim 1, Applicants assert that this rejection is moot. Specifically, claim 1, from which claim 11 depends, now recites the same definition of OX₇ that is recited in claim 11. Support for this amendment may be found on page 23, lines 10 – 13.

f) Not known what is meant by “heteroaryl” in definition of X₇

In light of the amendments to claim 11, Applicants assert that this rejection is moot. Specifically, Applicants have corrected the typographical error “heteroaryl.”

g) Not sufficient antecedent basis for “five-membered . . . aryl”

In light of the amendments to claim 11, Applicants assert that this rejection is moot. Specifically, claim 11 was amended to recite “five-membered . . . heteroaryl” thus correcting an obvious clerical error and the apparent lack of antecedent basis.

h) Not known what is meant by “heteroaryl” in definition of $R_3 - R_9$

In light of the amendments to claim 11, Applicants assert that this rejection is moot. Specifically, Applicants have corrected the typographical error “heteroaryl.”

(i) Not sufficient antecedent basis in claim 1 for definition of R_{13} and R_{14} in claim 11

In light of the amendments to claim 1, Applicants assert that this rejection is moot. Specifically, claim 1, from which claim 11 depends, now recites the definition of R_{13} and R_{14} recited in claim 11, which provides the proper antecedent basis.

(j) No Z or n in formula (V) in claims 12 and 28

In light of the amendments to claims 12 and 28, Applicants assert that this rejection is moot. Specifically, Applicants have deleted the definitions of Z and n from claims 12 and 28.

(k) Not sufficient antecedent basis in claim 1 for NX_1X_2

In light of the amendments to claim 12, Applicants assert that this rejection is moot. Specifically, claim 12 was amended such that the definitions for R_1 and R_2 recite NX_2X_3 , as in claim 1, and not NX_1X_2 .

(l) Not sufficient antecedent basis for “benzyl” in claim 1

In light of the amendments to claim 1, Applicants assert that this rejection is moot. Specifically, claim 1, from which claim 12 depends, now recites the term “benzyl” under the definition of R_1 and R_2 .

(m) Not sufficient antecedent basis in claim 1 for NX_3X_4

In light of the amendments to claim 12, Applicants assert that this rejection is moot. Specifically, claim 12 was amended such that the definitions for R_1 and R_2 recite NX_2X_3 , as in claim 1, and not NX_3X_4 .

(n) and (o) Not sufficient antecedent basis in claim 1 for $R_3 - R_6$ being attached to the pyrrole ring of a compound of formula (X)

In light of the amendments to claims 15 and 20, Applicants assert that this rejection is moot. Specifically, claims 15 and 20 now recite a compound where the variables on the pyrrole ring are $R_6 - R_9$ and not $R_3 - R_6$. The amendments to these claims were done to correct an obvious clerical error.

(p) Claim 16 and 32 do not end in a period

In light of the cancellation of claims 16 and 32, Applicants assert that this rejection is moot.

(q) Lack of paragraph break in claim 26

In light of the amendment to claim 26, thereby correcting the missing paragraph break, Applicants assert that this rejection is moot.

(r) Not known what is meant by R_{11} and R_{12} in claim 28

In light of the amendments to claim 28, Applicants assert that this rejection is moot. Specifically, Applicants have deleted the definitions R_{11} and R_{12} from claim 28 to correct an obvious clerical error.

(s) Not sufficient antecedent basis in claim 34 for "said second structure"

In light of the amendments 34, Applicants assert that this rejection is moot. Specifically, Applicants have amended claim 34 to recite "said second reactant."

(t) Not sufficient antecedent basis for "five-membered . . . aryl"

In light of the amendments to claim 34, Applicants assert that this rejection is moot. Specifically, claim 34 was amended to recite "five-membered . . . heteroaryl" thus correcting an obvious clerical error and the apparent lack of antecedent basis.

III. Rejection of Claims 26 – 28 and 31 – 33 Under 35 U.S.C. § 102

On page 11 of the Office Action, the Examiner rejected claims 26 – 28 and 31 – 33 under 35 U.S.C. § 102 as allegedly being anticipated by Shenoy, et al. (U.S. Patent No. 6,248,771).

In light of the amendments to claims 26 –28, Applicants assert that this rejection has been overcome. Applicants have excluded compound A-19, found on page 32 of the specification, from the scope of claims 26 – 28. *See In re Johnson* 558 F.2d 1008 (1977) (finding written description support for claim amendment to exclude species recited in application). Reconsideration and withdrawal are respectfully requested.

IV. Rejection of Claims 26 – 28 and 31 – 33 Under 35 U.S.C. § 103

On page 11 of the Office Action, the Examiner rejected claims 26 – 28 and 31 –33 under 35 U.S.C. § 103 as allegedly being rendered obvious by Shenoy, et al. (U.S. Patent No. 6,248,771).

Applicants submit that the Shenoy reference is not a competent reference for the purposes of an obviousness rejection under 35 U.S.C. § 103(a) since this application was filed on January 26, 2001; that is, after the inception of the amendments to 35 U.S.C. § 103 under the American Inventors Protection Act (AIPA) of 1999.

As amended, 35 U.S.C. § 103(c) states:

Subject matter developed by another person, which qualifies as prior art only under subsection (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

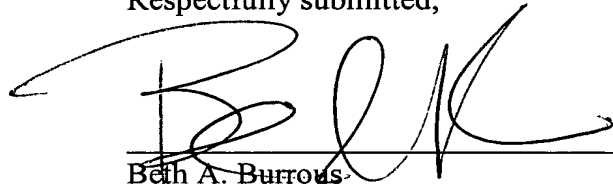
Applicants assert that the claimed invention and the Shenoy patent were commonly owned by Sugan, Inc. at the time the claimed invention was made. In support of this assertion, Applicants submit herewith a copy of the assignment document(s) for the Shenoy patent, which issued from U.S. Serial No. 09/034,734, and for the instant application. Thus, under the new law, the Shenoy patent may not be held as prior art, under 35 U.S.C. § 103, against the claimed invention. Accordingly, reconsideration and withdrawal of the § 103 rejection is respectfully requested.

V. Conclusion

In view of the above remarks and amendments, it is respectfully submitted that this application is in condition for allowance. Early notice to that effect is earnestly solicited. Examiner Coleman is invited to telephone the undersigned at the number listed below if she believes such would be helpful in advancing the application to issue.

6/30/03
Date

Respectfully submitted,


Beth A. Burrous
Reg. No. 35,087

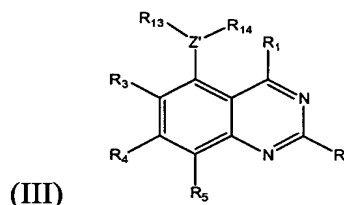
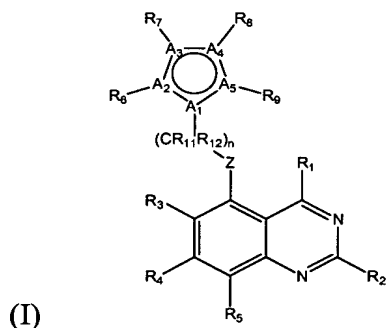
Foley & Lardner
3000 K Street, NW
Washington, DC 20007
Tel:(202) 672-5300
Fax:(202) 672-5399

Marked-up Claims:

1. (Twice amended) A method of modulating the function of a serine/threonine protein kinase with a quinazoline-based compound, comprising the step of contacting cells expressing said serine/threonine kinase with said compound, or a pharmaceutically acceptable salt thereof,

wherein said function of said serine/threonine protein kinase is related to cancer or fibrotic disorders; and

wherein said compound has the formula set forth in formula I or III:



wherein:

(a) Z is oxygen, NX_1 , or sulfur, where X_1 is selected from the group consisting of hydrogen, saturated or unsaturated alkyl, and five-membered or six-membered heteroaryl or six-membered aryl ring moieties;

(b) n is 0, 1, 2, 3, or 4;

(c) A_1 , A_2 , A_3 , A_4 and A_5 are independently selected from the group consisting of carbon, nitrogen, oxygen, and sulfur,

provided that if any of A_1 , A_2 , A_3 , A_4 and A_5 is nitrogen, oxygen, or sulfur, said A_1 , A_2 , A_3 , A_4 and A_5 is not substituted with R_6 , R_7 , R_8 or R_9 ;

A_1 is nitrogen or carbon;

(d) R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 and R_9 are independently selected from the group consisting of:

(i) hydrogen;

(ii) saturated or unsaturated alkyl;

(iii) NX_2X_3 , where X_2 and X_3 are independently selected from the group consisting of hydrogen, saturated or unsaturated alkyl, and five-membered or six-membered heteroaryl or six-membered aryl ring moieties;

(iv) benzyl;

(iv) halogen or trihalomethyl;

(vi) a ketone of formula $-\text{CO}-\text{X}_4$, where X_4 is selected from the group consisting of hydrogen, alkyl, and five-membered or six-membered heteroaryl or six-membered aryl ring moieties;

(vii) a carboxylic acid of formula $-(\text{X}_5)_{n5}-\text{COOH}$ or ester of formula $-(\text{X}_6)_{n6}-\text{COOX}_7$, where X_5 , X_6 , and X_7 are independently selected from the group consisting of alkyl and five-membered or six-membered heteroaryl or six-membered aryl ring moieties and where $n5$ and $n6$ are each independently 0 or 1;

(viii) an alcohol of formula $-(\text{X}_8)_{n8}-\text{OH}$ or an alkoxy moiety of formula $-(\text{X}_8)_{n8}-\text{OX}_9$, where X_8 and X_9 are independently selected from the group consisting of alkyl and five-membered or six-membered heteroaryl or six-membered aryl ring moieties and where $n8$ is 0 or 1, and where said ring moieties are optionally substituted with one or more substituents selected from the group consisting of alkyl, halogen, trihalomethyl, carboxylate, and ester;

(ix) $-\text{NHCOX}_{10}$, where X_{10} is selected from the group consisting of alkyl, hydroxyl, and five-membered or six-membered heteroaryl or six-membered aryl ring moieties, wherein said ring moieties are optionally substituted with one or more substituents selected from the group consisting of alkyl, halogen, trihalomethyl, carboxylate, and ester;

(x) $-\text{SO}_2\text{NX}_{11}\text{X}_{12}$, where X_{11} and X_{12} are selected from the group consisting of hydrogen, alkyl, and five-membered or six-membered heteroaryl or six-membered aryl ring moieties; and

(xi) a five-membered or six-membered heteroaryl or six-membered aryl ring moiety optionally substituted with one or more substituents selected from the group consisting of alkyl, halogen, trihalomethyl, carboxylate, and ester moieties;

(xii) $-\text{OX}_7$, where X_7 is selected from the group consisting of hydrogen, saturated or unsaturated alkyl, and a five-membered or six-membered aryl or heteroaryl ring moiety;

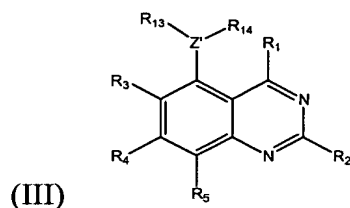
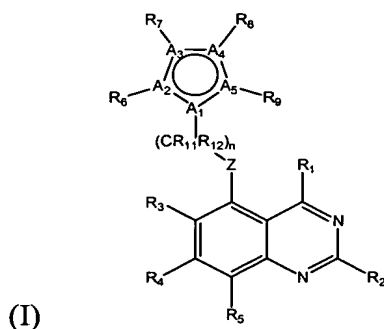
(e) any adjacent R_3 , R_4 , and R_5 or any adjacent R_6 , R_7 , R_8 , and R_9 are fused together to form a five-membered or six-membered heteroaryl or six-membered aryl ring moiety, wherein said five-membered or six-membered heteroaryl or six-membered aryl ring comprises two carbon atoms of said quinazoline-based compound ~~quinazoline ring~~ to which R_3 , R_4 , and R_5 or R_6 , R_7 , R_8 , and R_9 are attached; and

(f) R_{11} and R_{12} are independently selected from the group consisting of

- (i) hydrogen;
- (ii) saturated or unsaturated alkyl; and

(g) Z' is carbon, ~~oxygen, sulfur,~~ or nitrogen and R₁₃ and R₁₄ taken together form a five-membered or six-membered heteroaryl ring with Z' as a ring member, wherein said ring is optionally substituted with one, two or three alkyl, halogen, trihalomethyl, carboxylate, and ester moieties.

11. (Twice amended) The method of claim 1, wherein said quinazoline-based compound has the formula set forth in structure I or III:



wherein:

(a) Z is oxygen, NX₁, or sulfur, where X₁ is selected from the group consisting of hydrogen, and saturated or unsaturated alkyl;

(b) n is 0, 1, or 2;

(c) A₁, A₂, A₃, A₄ and A₅ are independently selected from the group consisting of carbon, nitrogen, oxygen, and sulfur,

provided that if any of A₁, A₂, A₃, A₄ and A₅ is nitrogen, oxygen, or sulfur, said A₁, A₂, A₃, A₄ and A₅ is not substituted with R₆, R₇, R₈ or R₉;

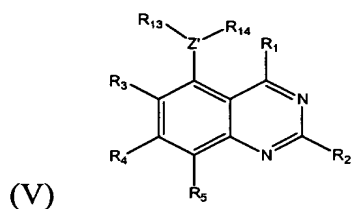
A₁ is carbon or nitrogen;

(d) R₁ and R₂ are independently selected from the group consisting of:

- (i) hydrogen;
- (ii) saturated or unsaturated alkyl;

- (iii) NX_2X_3 , where X_2 and X_3 are independently selected from the group consisting of hydrogen and saturated or unsaturated alkyl;
- (iv) halogen or trihalomethyl; and
- (v) five-membered or six-membered heteroaryl ring moiety;
- (e) R_3 , R_4 , R_5 , R_6 , R_7 , R_8 and R_9 are independently selected from the group consisting of:
- (i) hydrogen;
- (ii) saturated or unsaturated alkyl;
- (iii) NX_4X_5 , where X_4 and X_5 are independently selected from the group consisting of hydrogen and saturated or unsaturated alkyl;
- (iv) halogen or trihalomethyl; and
- (v) $C(X_6)_3$ where X_6 is selected from the group consisting of fluorine, chlorine, bromine and iodine; and
- (vi) $-OX_7$, where X_7 is selected from the group consisting of hydrogen, saturated or unsaturated alkyl, and a five-membered or six-membered aryl or heteroaryl ring moiety;
- (f) any adjacent R_3 , R_4 , and R_5 or any adjacent R_6 , R_7 , R_8 and R_9 are fused together to form a five-membered or six-membered aryl-heteroaryl or heteroaryl-six-membered aryl ring moiety, wherein said five-membered or six-membered aryl-heteroaryl or six-membered heteroaryl ring comprises two carbon atoms of said quinazoline-based compound the quinazoline ring to which R_3 , R_4 , and R_5 or R_6 , R_7 , R_8 , and R_9 are attached;
- (g) R_{11} and R_{12} are independently selected from the group consisting of
- (i) hydrogen;
- (ii) saturated or unsaturated alkyl; and
- (h) Z' is carbon, oxygen, sulfur, or nitrogen and R_{13} and R_{14} taken together form a five-membered or six-membered heteroaryl ring with Z' as a ring member, wherein said ring is optionally substituted with one, two, or three alkyl, halogen, trihalomethyl, carboxylate, and ester moieties.

12. (Twice amended) The method of claim 1, wherein said quinazoline-based compound has the formula set forth in formula V:



wherein:

~~—— (a) Z is oxygen or sulfur;~~

~~—— (b) n is 0 or 1;~~

(ea) R₁ and R₂ are independently selected from the group consisting of:

(i) hydrogen;

(ii) $\text{NX}_1\text{X}_2\text{NX}_2\text{X}_3$, where X₂₄ and X₃₂ are independently selected from the group consisting of hydrogen and saturated or unsaturated alkyl; and

(iii) benzyl;

(db) R₃, R₄, and R₅ are independently selected from the group consisting of:

(i) hydrogen; and

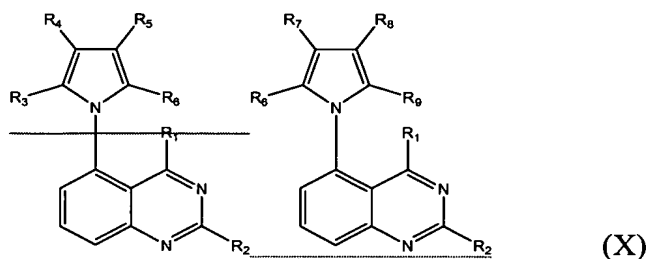
(ii) saturated or unsaturated alkyl; and

(iii) $\text{NX}_3\text{X}_4\text{NX}_2\text{X}_3$, where X₂₃ and X₃₄ are independently selected from the group consisting of hydrogen and saturated or unsaturated alkyl; and

~~—— (e) R₁₁ and R₁₂ hydrogen; and~~

(fc) Z' is nitrogen and R₁₃ and R₁₄ taken together form a five-membered heteroaryl ring.

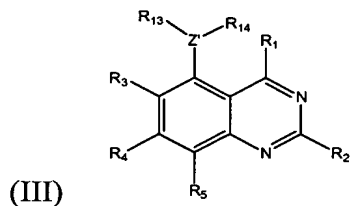
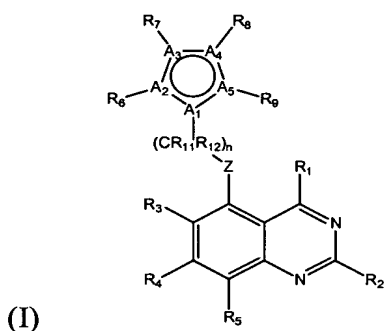
15. (Amended) The method of claim 1, wherein said quinazoline-based compound has a structure set forth in formula X:



wherein

- (a) R_1 and R_2 are independently selected from the group consisting of hydrogen, $-NH_2$, provided at least one of R_1 and R_2 is $-NH_2$;
- (b) R_{63} , R_{74} , R_{85} , and R_{96} are independently selected from the group consisting of
- (i) hydrogen;
 - (ii) saturated or unsaturated alkyl;
 - (iii) $NX_4X_5NX_2X_3$, where X_4-X_2 and X_5-X_3 are independently selected from the group consisting of hydrogen and saturated or unsaturated alkyl; and
 - (iv) halogen;
 - (v) $C(X_6)_3$, where X_6 is selected from the group consisting of fluorine, chlorine, bromine, and iodine; and
 - (vi) OX_7 , where X_7 is selected from the group consisting of hydrogen, saturated or unsaturated alkyl, and a five-membered or six-membered aryl or heteroaryl ring moiety.

17. (Twice amended) A method of ~~preventing or treating~~ an abnormal condition in an organism in need thereof, wherein said abnormal condition is a disease associated with an aberration in a signal transduction pathway characterized by an interaction between a serine/threonine protein kinase and a natural binding partner, said method comprising the step of administering a quinazoline-based compound of formula I or III to said organism:



wherein:

(a) Z is oxygen, NX_1 , or sulfur, where X_1 is selected from the group consisting of hydrogen, saturated or unsaturated alkyl, and five-membered or six-membered heteroaryl or six-membered aryl ring moieties;

(b) n is 0, 1, 2, 3, or 4;

(c) A_1 , A_2 , A_3 , A_4 and A_5 are independently selected from the group consisting of carbon, nitrogen, oxygen, and sulfur,

provided that if any of A_1 , A_2 , A_3 , A_4 and A_5 is nitrogen, oxygen, or sulfur, said A_1 , A_2 , A_3 , A_4 and A_5 is not substituted with R_6 , R_7 , R_8 or R_9 ;

A_1 is carbon or nitrogen;

(d) R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 and R_9 are independently selected from the group consisting of:

(i) hydrogen;

(ii) saturated or unsaturated alkyl;

(iii) NX_2X_3 , where X_2 and X_3 are independently selected from the group consisting of hydrogen, saturated or unsaturated alkyl, and five-membered or six-membered heteroaryl or six-membered aryl ring moieties;

(iv) halogen or trihalomethyl;

(v) a ketone of formula $-CO-X_4$, where X_4 is selected from the group consisting of hydrogen, alkyl, and five-membered or six-membered heteroaryl or six-membered aryl ring moieties;

(vi) a carboxylic acid of formula $-(X_5)_{n5}-COOH$ or ester of formula $-(X_6)_{n6}-COOX_7$, where X_5 , X_6 , and X_7 are independently selected from the group consisting of alkyl and five-membered or six-membered heteroaryl or six-membered aryl ring moieties and where $n5$ and $n6$ are each independently 0 or 1;

(vii) an alcohol of formula $-(X_8)_{n8}-OH$ or an alkoxy moiety of formula $-(X_8)_{n8}-OX_9$, where X_8 and X_9 are independently selected from the group consisting of alkyl and five-membered or six-membered heteroaryl or six-membered aryl ring moieties and where $n8$ is 0 or 1, and where said ring moieties are optionally substituted with one or more substituents selected from the group consisting of alkyl, halogen, trihalomethyl, carboxylate, and ester;

(viii) $-NHCOX_{10}$, where X_{10} is selected from the group consisting of alkyl, hydroxyl, and five-membered or six-membered heteroaryl or six-membered aryl ring moieties, wherein said ring moieties are optionally substituted with one or more substituents selected from the group consisting of alkyl, halogen, trihalomethyl, carboxylate, and ester;

(ix) $-\text{SO}_2\text{NX}_{11}\text{X}_{12}$, where X_{11} and X_{12} are selected from the group consisting of hydrogen, alkyl, and five-membered or six-membered heteroaryl or six-membered aryl ring moieties; and

(x) a five-membered or six-membered heteroaryl or six-membered aryl ring moiety optionally substituted with one or more substituents selected from the group consisting of alkyl, halogen, trihalomethyl, carboxylate, and ester moieties;

(e) any adjacent R_3 , R_4 , and R_5 or any adjacent R_6 , R_7 , R_8 , and R_9 are fused together to form a five-membered or six-membered heteroaryl or six-membered aryl ring moiety, wherein said five-membered or six-membered heteroaryl or six-membered aryl ring comprises two carbon atoms of said quinazoline-based compound ~~the quinoxaline ring~~ to which R_3 , R_4 , and R_5 or R_6 , R_7 , R_8 , and R_9 are attached; ~~and~~

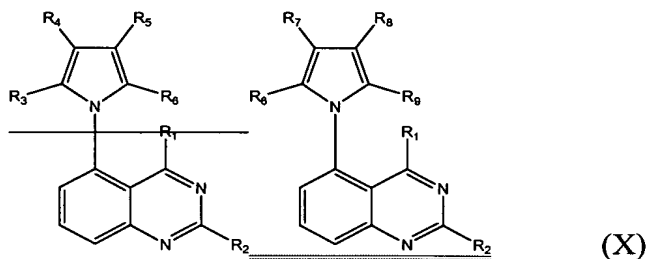
(f) R_{11} and R_{12} are independently selected from the group consisting of

(i) hydrogen;

(ii) saturated or unsaturated alkyl; and

(g) Z' is carbon, ~~oxygen, sulfur,~~ or nitrogen and R_{13} and R_{14} taken together form a five-membered or six-membered heteroaryl ring with Z' as a ring member.

20. (Amended) The method of claim 17, wherein said quinazoline-based compound has a structure set forth in formula X:



wherein

(a) R_1 and R_2 are independently selected from the group consisting of hydrogen and $-\text{NH}_2$, provided at least one of R_1 and R_2 is $-\text{NH}_2$;

(b) R_{63} , R_{74} , R_{85} , and R_{96} are independently selected from the group consisting of

(i) hydrogen;

(ii) saturated or unsaturated alkyl;

(iii) $\text{NX}_4\text{X}_5\text{NX}_2\text{X}_3$, where X_4X_2 and X_5X_3 are independently selected from the group consisting of hydrogen and saturated or unsaturated alkyl; ~~and~~

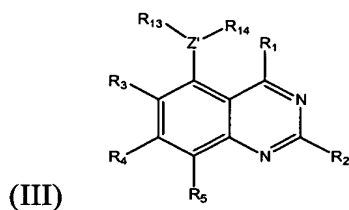
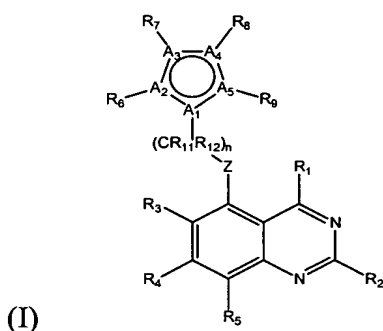
(iv) halogen;

(v) $C(X_6)_3$, where X_6 is selected from the group consisting of fluorine, chlorine, bromine, and iodine; and

(vi) OX_7 , where X_7 is selected from the group consisting of hydrogen, saturated or unsaturated alkyl, and a five-membered or six-membered aryl or heteroaryl ring moiety.

23. (Amended) The method of claim 22~~1~~, wherein said ~~abnormal condition is a~~ cancer is selected from the group consisting of lung cancer, ovarian cancer, breast cancer, brain cancer, intra-axial brain cancer, colon cancer, prostate cancer, Kaposi's sarcoma, melanoma, and glioma.

26. (Twice amended) A quinazoline compound having the formula I or III:



wherein:

(i) Z is oxygen, NX_1 , or sulfur, where X_1 is selected from the group consisting of hydrogen, saturated or unsaturated alkyl, and five-membered or six-membered heteroaryl or six-membered aryl ring moieties;

(ii) n is 0, 1, 2, 3, or 4;

(iii) A_1 , A_2 , A_3 , A_4 and A_5 are independently selected from the group consisting of carbon, nitrogen, oxygen, and sulfur,

provided that if any of A_1 , A_2 , A_3 , A_4 and A_5 is nitrogen, oxygen, or sulfur, said A_1 , A_2 , A_3 , A_4 and A_5 is not substituted with R_6 , R_7 , R_8 or R_9 ;

A_1 is carbon or nitrogen;

(iv) R_1 and R_2 are independently selected from the group consisting of:

(a) hydrogen;
 (b) saturated or unsaturated alkyl;
 (c) NX_2X_3 , where X_2 and X_3 are independently selected from the group consisting of hydrogen and saturated or unsaturated alkyl;
 (d) halogen or trihalomethyl; and
 (e) five-membered or six-membered heteroaryl ring moiety;
 (v) R_3 , R_4 , R_5 , R_6 , R_7 , R_8 and R_9 are independently selected from the group consisting of:

(a) hydrogen;
 (b) saturated or unsaturated alkyl;
 (c) $NX_{13}X_{14}$, where X_{13} and X_{14} are independently selected from the group consisting of hydrogen, saturated or unsaturated alkyl, and five-membered or six-membered aryl or heteroaryl ring moieties;
 (d) halogen or trihalomethyl;
 (e) a ketone of formula $-CO-X_4$, where X_4 is selected from the group consisting of hydrogen, alkyl, and five-membered or six-membered heteroaryl or six-membered aryl ring moieties;
 (f) a carboxylic acid of formula $-(X_5)_{n5}-COOH$ or ester of formula $-(X_6)_{n6}-COOX_7$, where X_5 , X_6 , and X_7 are independently selected from the group consisting of alkyl and five-membered or six-membered heteroaryl or six-membered aryl ring moieties and where $n5$ and $n6$ are each independently 0 or 1;
 (g) an alcohol of formula $-(X_8)_{n8}-OH$ or an alkoxy moiety of formula $-(X_8)_{n8}-OX_9$, where X_8 and X_9 are independently selected from the group consisting of alkyl and five-membered or six-membered heteroaryl or six-membered aryl ring moieties and where $n8$ is 0 or 1, and where said ring moieties are optionally substituted with one or more substituents selected from the group consisting of alkyl, halogen, trihalomethyl, carboxylate, and ester;
 (h) $-NHCOX_{10}$, where X_{10} is selected from the group consisting of alkyl, hydroxyl, and five-membered or six-membered heteroaryl or six-membered aryl ring moieties, wherein said ring moieties are optionally substituted with one or more substituents selected from the group consisting of alkyl, halogen, trihalomethyl, carboxylate, and ester;
 (i) $-SO_2NX_{11}X_{12}$, where X_{11} and X_{12} are selected from the group consisting of hydrogen, alkyl, and five-membered or six-membered heteroaryl or six-membered aryl ring moieties; and

(j) a five-membered or six-membered heteroaryl or six-membered aryl ring moiety optionally substituted with one or more substituents selected from the group consisting of alkyl, halogen, trihalomethyl, carboxylate, and ester moieties;

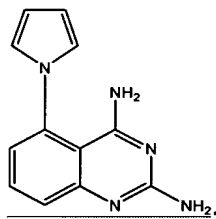
(vi) any adjacent R_3 , R_4 , and R_5 or any adjacent R_6 , R_7 , R_8 , and R_9 are fused together to form a five-membered or six-membered heteroaryl or six-membered aryl ring moiety, wherein said five-membered or six-membered heteroaryl or six-membered aryl ring comprises two carbon atoms of said quinazoline compound ~~the quinazoline ring~~ to which R_3 , R_4 , and R_5 or R_6 , R_7 , R_8 , and R_9 are attached;

(vii) R_{11} and R_{12} are independently selected from the group consisting of

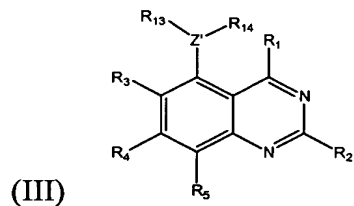
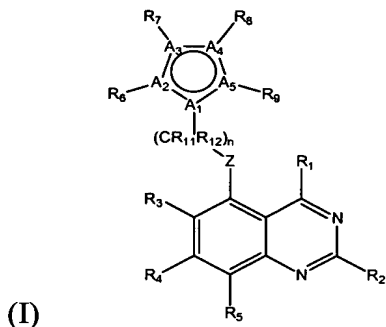
(i) hydrogen;

(ii) saturated or unsaturated alkyl; and

(viii) Z' is carbon, ~~oxygen, sulfur,~~ or nitrogen and R_{13} and R_{14} taken together form a five-membered or six-membered heteroaryl ring with Z' as a ring member; with the proviso that the compound of formula (I) or (III) is not



27. (Twice amended) A quinazoline compound having the formula I or III:



wherein:

(a) Z is oxygen, NX_1 , or sulfur, where X_1 is selected from the group consisting of hydrogen, and saturated or unsaturated alkyl;

(b) n is 0, 1, or 2;

(c) A_1 , A_2 , A_3 , A_4 and A_5 are independently selected from the group consisting of carbon, nitrogen, oxygen, and sulfur,

provided that if any of A_1 , A_2 , A_3 , A_4 and A_5 is nitrogen, oxygen, or sulfur, said A_1 , A_2 , A_3 , A_4 and A_5 is not substituted with R_6 , R_7 , R_8 or R_9 ;

A_1 is carbon or nitrogen;

(d) R_1 and R_2 are independently selected from the group consisting of:

(i) hydrogen;

(ii) saturated or unsaturated alkyl;

(iii) NX_2X_3 , where X_2 and X_3 are independently selected from the group consisting of hydrogen and saturated or unsaturated alkyl;

(iv) halogen or trihalomethyl; and

(v) five-membered or six-membered heteroaryl ring moiety;

(e) R_3 , R_4 , R_5 , R_6 , R_7 , R_8 and R_9 are independently selected from the group consisting of:

(i) hydrogen;

(ii) saturated or unsaturated alkyl;

(iii) NX_4X_5 , where X_4 and X_5 are independently selected from the group consisting of hydrogen and saturated or unsaturated alkyl;

(iv) halogen or trihalomethyl;

(v) $C(X_6)_3$, where X_6 is selected from the group consisting of fluorine, chlorine, bromine and iodine;

(vi) $-OX_7$, where X_7 is selected from the group consisting of hydrogen, saturated or unsaturated alkyl, and a five-membered or six-membered aryl or ~~heteroaryl~~heteroaryl ring moiety;

(f) any adjacent R_3 , R_4 , and R_5 or any adjacent R_6 , R_7 , R_8 and R_9 are fused together to form a five-membered or six-membered ~~aryl~~heteroaryl or ~~heteroaryl~~six-membered aryl ring moiety, wherein said five-membered or six-membered aryl or six-membered heteroaryl ring comprises two carbon atoms of said quinazoline compound ~~the quinazoline ring~~ to which R_3 , R_4 , and R_5 or R_6 , R_7 , R_8 , and R_9 are attached;

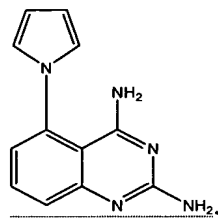
(g) R_{11} and R_{12} are independently selected from the group consisting of

(i) hydrogen; and

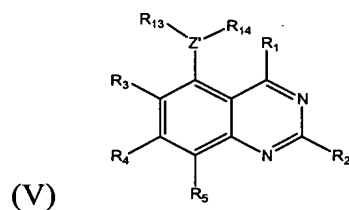
(ii) saturated or unsaturated alkyl; and

(h) ~~Z' is carbon, nitrogen, oxygen, sulfur, or nitrogen~~ and R_{13} and R_{14} taken together form a five-membered or six-membered heteroaryl ring with Z' as a ring member, wherein said ring is optionally substituted with one, two, or three alkyl, halogen, trihalomethyl, carboxylate, and ester moieties;

with the proviso that the compound of formula (I) or (III) is not



28. (Twice amended) A quinazoline compound having the structure set forth in formula V:



wherein:

~~(a) Z is oxygen or sulfur;~~

~~(b) n is 0 or 1;~~

(e*a*) R_1 and R_2 are independently selected from the group consisting of:

(i) hydrogen;

(ii) NX_1X_2 , where X_1 and X_2 are independently selected from the group consisting of hydrogen and saturated or unsaturated alkyl; and

(iii) benzyl;

(e*b*) R_3 , R_4 , and R_5 are independently selected from the group consisting of:

(i) hydrogen;

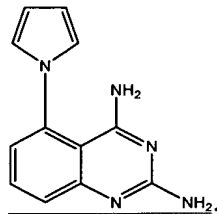
(ii) saturated or unsaturated alkyl; and

(iii) NX_3X_4 , where X_3 and X_4 are independently selected from the group consisting of hydrogen and saturated or unsaturated alkyl;

~~(e) R₁₁ and R₁₂ hydrogen; and~~

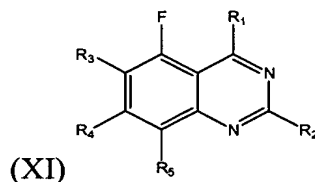
~~(f) Z' is nitrogen and R₁₃ and R₁₄ taken together form a five-membered heteroaryl ring;~~

with the proviso that the compound of formula (V) is not

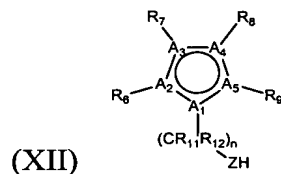


34. (Twice amended) A method for synthesizing a compound of claim 26, comprising the steps of:

(a) reacting a first reactant with a second reactant to yield said compound, wherein said first reactant has a structure of formula XI:



and wherein said second ~~structure~~ reactant has a structure of formula (XII):



wherein,

(a) Z is oxygen or sulfur;

(b) n is 0, 1, 2, 3, or 4;

(c) A₁-A₂, A₃, A₄, and A₅ are independently selected from the group consisting of carbon, nitrogen, oxygen, and sulfur,

provided that if any of A₁-A₂, A₃, A₄ and A₅ is nitrogen, oxygen, or sulfur, said A₁-A₂, A₃, A₄ and A₅ is not substituted with R₆, R₇, R₈ or R₉;

A₁ is carbon or nitrogen;

(d) R_1 and R_2 are independently selected from the group consisting of:

- (i) hydrogen;
- (ii) saturated or unsaturated alkyl;
- (iii) NX_2X_3 , where X_2 and X_3 are independently selected from the group consisting of hydrogen, and saturated or unsaturated alkyl;
- (iv) halogen or trihalomethyl; and
- (v) five-membered or six-membered heteroaryl ring moiety;

(e) R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , and R_9 are independently selected from the group consisting of:

- (i) hydrogen;
- (ii) saturated or unsaturated alkyl;
- (iii) $NX_{13}X_{14}$, where X_{13} and X_{14} are independently selected from the group consisting of hydrogen, saturated or unsaturated alkyl, and five-membered or six-membered aryl or heteroaryl ring moieties;
- (iv) halogen or trihalomethyl;
- (v) a ketone of formula $-CO-X_4$, where X_4 is selected from the group consisting of hydrogen, alkyl, and five-membered or six-membered heteroaryl or six-membered aryl ring moieties;
- (vi) a carboxylic acid of formula $-(X_5)_{n5}-COOH$ or ester of formula $-(X_6)_{n6}-COOX_7$, where X_5 , X_6 , and X_7 are independently selected from the group consisting of alkyl and five-membered or six-membered heteroaryl or six-membered aryl ring moieties and where $n5$ and $n6$ are 0 or 1;
- (vii) an alcohol of formula $-(X_8)_{n8}-OH$ or an alkoxy moiety of formula $-(X_8)_{n8}-OX_9$, where X_8 and X_9 are independently selected from the group consisting of alkyl and five-membered or six-membered heteroaryl or six-membered aryl ring moieties and where $n8$ is 0 or 1, and where said ring moieties are optionally substituted with one or more substituents selected from the group consisting of alkyl, halogen, trihalomethyl, carboxylate, and ester;
- (viii) $-NHCOX_{10}$, where X_{10} is selected from the group consisting of alkyl, hydroxyl, and five-membered or six-membered heteroaryl or six-membered aryl ring moieties, wherein said ring moieties are optionally substituted with one or more substituents selected from the group consisting of alkyl, halogen, trihalomethyl, carboxylate, and ester;

(ix) $-\text{SO}_2\text{NX}_{11}\text{X}_{12}$, where X_{11} and X_{12} are selected from the group consisting of hydrogen, alkyl, and five-membered or six-membered heteroaryl or six-membered aryl ring moieties; and

(x) a five-membered or six-membered heteroaryl or six-membered aryl ring moiety optionally substituted with one or more substituents selected from the group consisting of alkyl, halogen, trihalomethyl, carboxylate, and ester moieties;

(f) any adjacent R_3 , R_4 , and R_5 or any adjacent R_6 , R_7 , R_8 , and R_9 are fused together ~~for to~~ form a five-membered or six-membered heteroaryl or or six-membered arylheteroaryl ring moiety wherein said five-membered or six-membered heteroaryl or six-membered heteroaryl ring comprises two carbon atoms of the ~~quinazoline~~ ring to which R_3 , R_4 , and R_5 or R_6 , R_7 , R_8 , and R_9 are attached;

(g) R_{11} and R_{12} are independently selected from the group consisting of

(i) hydrogen; and

(ii) saturated or unsaturated alkyl; and

(b) collecting a precipitate comprising said compound.